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## Abbreviated breast MRI (FAST MRI) interpretation

**Title:** Can mammogram-readers swiftly and effectively learn to interpret First post contrast Acquisition Subtracted (FAST) MRI, a type of abbreviated breast MRI? - A single centre data-interpretation study

**Running title:** Abbreviated breast MRI (FAST MRI) interpretation

**Key words:** Breast cancer; screening; early diagnosis; imaging biomarker; abbreviated breast MRI; training

### **Abbreviations:**

FAST MRI	First postcontrast Acquisition SubTracted breast Magnetic Resonance Imaging (a type of abbreviated breast MRI)
MR or MRI	Magnetic Resonance Imaging
MIP	Maximum Intensity Projection image of combined stack of subtracted slices
NHS	National Health Service
NHSBSP	National Health Service Breast Screening Programme

## Abstract

**Objectives:** To assess whether NHS breast screening programme (NHSBSP) mammogram readers could effectively interpret First post contrast Acquisition SubTracted (FAST) MRI, for intended use in screening for breast cancer.

**Methods:** Eight NHSBSP mammogram readers from a single centre (4 who also read breast MRI (Group 1) and 4 who do not (Group 2)) were given structured FAST-MRI reader training (median 4 hours: 32 minutes). They then prospectively interpreted 125 FAST MRIs (250 breasts: 194 normal and 56 cancer) comprising a consecutive series of screening MRIs enriched with additional cancer cases from 2015, providing 2000 interpretations. Readers were blinded to other readers' opinions and to clinical information. Categorisation followed the NHSBSP MRI reporting categorisation, with categories 4 and 5 considered indicative of cancer. Diagnostic accuracy (reference standard: histology or 2 years' follow up) and agreement between readers were determined.

**Results:** The accuracy achieved by Group 2 (847/1000 (85%; 95% confidence interval (CI) 82-87%)) was 5% less than that achieved by Group 1 (898/1000 (90%; 95% CI 88-92)). Good inter-reader agreement was seen between both Group 1 readers ( $\kappa=0.66$ ; 95% CI 0.61-0.71) and Group 2 readers ( $\kappa=0.63$ ; 95% CI 0.58-0.68). The median time taken to interpret each abbreviated MRI was Group 1: 34 seconds (range 3-351) and Group 2: 77 (range 11-321).

**Conclusion:** Brief structured training enabled multi-professional mammogram readers to achieve similar accuracy at FAST MRI interpretation to consultant radiologists experienced at breast MRI interpretation.

**Advances in knowledge:** FAST MRI could be feasible from a training-the-workforce perspective for screening within NHSBSP.

**Key Words:** Breast cancer, Early diagnosis, Screening, Abbreviated breast MRI, Imaging biomarker, Training

## Introduction

Mammographic screening programmes result in both over-diagnosis and under-diagnosis of breast cancer(1–3). Under-diagnosis leads to cancers presenting symptomatically between screening visits (interval cancers), and to continued presentation of Stage 2 or greater breast cancers(4). Although magnetic resonance imaging (MRI) is the most sensitive method to detect breast cancer, currently only women classified as high risk (>30% lifetime risk) are offered screening MRI in the UK(5). However, in the future, personalised screening could enable larger numbers of women to be offered different screening regimes, each incorporating different imaging modalities, according to their level of risk(6,7).

Finding breast cancer early saves lives(8,9), and there is therefore a need to develop cost-effective imaging tests that will benefit women at risk of breast cancer by finding significant disease early(10). First post contrast Acquisition SubTracted (FAST) MRI is a type of abbreviated breast MRI and has been suggested as such a screening test since proof of concept studies suggest it could offer accuracy of breast cancer detection almost equivalent to full protocol breast MRI with speed of acquisition and reporting that approaches that of mammography (11–13). This technique might especially benefit women with dense breasts since cancers obscured by dense tissue on mammograms are often visible on MRI(14).

Mammographic population screening for breast cancer necessitates a high volume of throughput of images for interpretation, and in many countries radiologists who interpret mammograms do not necessarily also interpret breast MRI, a less frequently performed and more complex modality. In the UK, skills-mix has enabled professionals other than radiologists, including advanced practitioner radiographers, to learn to interpret screening mammograms and studies demonstrate their adequacy of performance at this task(15,16). The present study is the first to look at the capability of mammogram readers in the context of FAST MRI interpretation. FAST MRI was the new technology chosen for this study because it is the MR sequence common to most reported types of abbreviated protocol, with the shortest reported interpretation time and simplest format(11). In the design of this study, the authors postulated that its simplicity and the similarities of display between it and mammographic modalities would be likely to enable mammogram readers to easily and quickly learn FAST MRI interpretation. In the current study we chose to further simplify the display protocol, and unlike in Kuhl's original description of FAST MRI(11), the unsubtracted images were not made available for interpretation by our readers. This simplification of the display protocol was intended to ease training of mammogram readers, unfamiliar with multiple sequences.

The aim of this study was to explore whether NHSBSP mammogram readers can learn to effectively interpret FAST MRI with less than one day's additional training, and to match the capabilities of expert breast MRI readers at this task in terms of accuracy and speed of interpretation.

## Methods and Materials

Research Ethics Committee and Health Research Authority approval were obtained (references: REC 17/SW/0142, IRAS 219332). Informed consent was obtained from all study participants.

### Study design

Prospective, blinded interpretation by multiple readers of an enriched dataset with known outcome.

### Test set of Images

A set of FAST MRI examinations was created by copying and reducing (post-processing) breast MRI scans that were acquired at a single centre during 2015. MRIs were acquired exclusively during a single year in order to standardise scan quality. A consecutive sample of all breast MRIs performed as screening for women at high risk of breast cancer according to NICE guidelines (>30% lifetime risk from the age of 20 years) (5) were included (72 MRIs). These were enriched with 54 symptomatic MRIs including 1 with bilateral cancer and 53 with unilateral cancer (Figure 1). Two of the screening MRIs also showed a unilateral cancer. The clinical indications given for the 125 MRI scans that were included in the dataset are shown in Table 1. In order to increase task difficulty, only cancers smaller than 25mm were included, as measured on the original full MRI report. All cancer cases were confirmed by histological analysis of breast tissue. The histology of the 56 cancers in the dataset is shown in Table 2. Breasts were classified as not having cancer through either negative interpretation of full MRI by at least one fully trained radiologist or uncertain interpretation of full MRI and negative ultrasound (+/- biopsy), and at least 2 years' follow up data without cancer.

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The median age of the women imaged was 40 years (range 28-61) in the high-risk screening population and 58 (35-83) for the women with a new cancer diagnosis.

### Breast MRI protocol

All MRI examinations in the dataset were originally acquired on either a Philips (Amsterdam, Netherlands) Ingenia 1.5T or a Philips Ingenia 3T scanner. The breast coils used were dStream Breast 7 channel coils. The paramagnetic contrast agent used was gadobutrol 1.0mmol/ml and the dose administered was 0.1 millilitre gadobutrol per kg body weight (for example, a patient weighing 70kg would require a dose of 7 millilitres). The dynamic sequence used (from which the dataset's FAST MRI images were obtained through post-processing) was dyn\_eTHRIVE (Axial 3D T1 fast field echo (FFE)). Since the images used in the current study were originally acquired in 2015 and then later reprocessed and anonymised for the study, the acquisition protocol conformed to our own centre's standard. This differed from Kuhl's description of FAST MRI(11) as follows:

- The breasts were not compressed during MR acquisition.
- The T1 images of the dynamic study that were used to form the subtracted images were fat-suppressed (dyn\_eTHRIVE).

The MRI scans performed for a screening indication were performed during day 6-16 of the woman's menstrual cycle, but those performed post cancer diagnosis were performed promptly without reference to the woman's menstrual cycle.

The MRI studies were copied, anonymised and allocated study identifiers chronologically for the date they were acquired, and as a consequence normal and abnormal scans were presented to the readers in an unpredictable order. They were then reduced to comprise

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simply those MR sequences that would have been obtained if they had originally been acquired as a FAST MRI, displayed as an axial maximum intensity projection image (MIP), and also as a stack of axial slices (slice stack) of the first post contrast subtracted images from the dynamic series of the breast MRI examination(11). This process was performed by two of the research team who were not subsequently part of either of the two reading groups. These subtracted images alone comprised the FAST MRI scans interpreted by the readers.

### Study Participants

Eight radiology practitioners from a single centre were recruited as image readers; all practised as NHSBSP mammogram readers. These 8 practitioners comprised 4 readers who also practised as NHSBSP breast MRI readers (Group 1) and 4 readers who did not read breast MRI in their normal clinical practice (Group 2). Group 1 were all consultant radiologists with between 4 and 11 years' experience of reading both mammograms and breast MRIs. Individual members of Group 1 read between 5000 and 6,500 mammograms and between 100 and 225 breast MRIs each year. Group 2 comprised a consultant radiologist, a consultant radiographer and two film reading radiographers, with individual experience of reading mammograms ranging from 2 to 28 years and each member of Group 2 read between 5000 and 18,000 mammograms each year.



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### Standardised Training

All 8 readers were trained to read FAST MRI using a structured training package (17) including one-to-one training and interactive small group presentation components. All readers were then offered an additional one-to-one teaching session if they felt they would benefit. The examples of FAST MRI shown to the readers during the training were not from the subsequently interpreted dataset.

The structured training delivered during the present study to all-but-one reader took half a day to deliver. One reader (Reader Identifier 2.2) requested further training and this was delivered as a second one-to-one session, lasting one hour, when the reading task was four fifths completed.

Once trained, each reader completed a data-form for each FAST MRI case within the dataset, blinded to the identity of the patient, clinical history, original full MRI, all other imaging including mammograms, ultrasounds and previous breast MRI examinations, the outcome (cancer or no cancer) and to the opinions and completed data forms of the other readers. The FAST MRI case studies were read in batches of up to 25 because the workstation that displayed the images had a limited capacity for data-storage and was also required for routine clinical work.

### Classification system

The readers were instructed to classify each breast of each FAST MRI examination in accordance with a modified version of the MRI screening reporting categories of classification outlined in the 2012 NHSBSP guidelines for screening higher risk women, where MRI1 and MRI2 indicate normal and benign, MRI3 indicates an indeterminate

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classification, and MRI4 and MRI5 indicate suspicious and definitely malignant appearances respectively(18). The recommended MRI screening reporting categories were modified because FAST MRI differs from the full diagnostic protocol in providing limited morphological information and only a single time-point from the dynamic scan.

### Statistical Analysis

A per breast analysis of the frequency of MRI classifications against the true outcome was obtained overall and for each reader. The overall accuracy, sensitivity, specificity, false positive and negative rates (with total reads as denominator) and the positive and negative predictive values of the readers' MRI classification with the true outcome were calculated. Differences in accuracy, sensitivity and specificity across reader groups were analysed using a multilevel generalised mixed model to account for multiple readers per case. The inter-reader variability and the agreement between readers and the true outcome was assessed using Cohen's kappa coefficient to account for the probability of the agreement occurring by chance. A kappa statistic value of greater than 0.60 would represent good agreement. An MRI classification of 4 and 5 was considered indicative of cancer, and classifications of 1-3 considered a normal result. A sensitivity analysis was performed whereby those with an indeterminate classification MRI 3 were classified as cancer. The FAST MRI interpretation times were compared across reader groups using a Wilcoxon signed rank test and the reader training times compared using a Wilcoxon rank sum test.

## Results

All 8 readers completed the reading task of 125 cases (250 breasts). Per breast analysis comparing the readers' MRI classification with the true outcome (cancer or normal) showed an overall concordance with the true outcome of 87% (95% confidence interval (CI) 86-89%; 1745/2000 reads), with 393 (88%) cancers correctly identified and 1352 (87%) normal results correctly identified (Table 3). The overall sensitivity was 88% (95% CI 84-91%) and specificity 87% (95% CI 85-89%) (Table 4). The agreement between all readers and the true outcome demonstrated good concordance with a kappa of 0.69 (95% CI 0.65-0.72).

The concordance with the true outcome achieved by Group 2 (847/1000 (85%; 95% CI 82-87%)) was 5% less than that achieved by Group 1 (898/1000 (90%; 88-92%)) (Table 5), a small but significant difference ( $p < 0.0001$ ). Results for readers in Group 2 showed a non-significant trend towards higher sensitivity (89%; 95% CI 85-93%) but significantly lower specificity (83%; 95% CI 81-86%) than for readers in Group 1 (sensitivity 86%; 95% CI 81-90%,  $p = 0.23$ ; specificity 91%; 95% CI 89-93%,  $p < 0.0001$ ). Good inter-reader agreement was observed between the Group 1 readers (kappa=0.66; 95% CI 0.61-0.71) and also between the Group 2 readers (kappa=0.63; 95% CI 0.58-0.68) (Table 5).

A sensitivity analysis considering MRI classifications 3, 4 and 5 to indicate cancer gave an overall accuracy of 78% (1550/2000; 95% CI 76-79%; Table 4).

### Time taken to report

The time taken for the individual readers to interpret each FAST MRI examination was significantly less for Group 1 (median 34 seconds, range 3-351 seconds) than for Group 2 (77 seconds, 11-321 seconds,  $p < 0.0001$ ).

### Time taken to train

It took less than one day of structured training to train the readers in this study. The training time between groups was not significantly different (median training time 4:01 (hours:minutes) and range 3:25–4:42) for Group 1, and 4:55 (4:25-6:04) for Group 2,  $p=0.11$ ).

## Discussion

Following less than one day's structured training the NHSBSP mammogram readers in this study achieved a good agreement between their interpretation of FAST MRI and the clinically proven outcome in this enriched dataset. The group with no previous experience of breast MRI performed just 5% less well in terms of overall accuracy in comparison with the group of expert breast MRI readers. Looking at the individual accuracy for the readers within each group (Table 4), there is some overlap between groups: the lowest accuracy in Group 1 of 86% is lower than the accuracy of the two best performing readers in Group 2.

The median time taken to interpret FAST MRI by individual readers in Group 1 ranged from 27-44 seconds with a median for the whole group of 33 seconds. This is similar to the 28 seconds taken by expert readers in Kuhl's original proof of concept publication(11). For Group 2 the range was 57-144 with a median for the whole group of 77 seconds, double that of Group 1. This significant difference between groups may indicate that following training, new readers of FAST MRI may take time to achieve the same reading speed as experienced MRI readers.

A UK workplace-based double module in breast MRI reporting, as part of an MSc in Clinical Reporting for Radiographers and Breast Clinicians, has recently been established, designed

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for professionals already competent in both mammogram interpretation and breast ultrasound performance. It includes a logbook of 200 breast MRI examinations reported by the trainee and requires a radiologist to mentor each participant during the 9 month course. This course successfully achieves acceptable competency levels(19), but the complexity and length of the course make it impractical for training the whole image-reading workforce, for both manpower and financial reasons. In contrast, the interpretation of digital breast tomosynthesis can be effectively learnt by a professional competent at mammogram interpretation, within a single structured day of study(20).

Interestingly, the readers in this study achieved a better match in terms of overall accuracy when MRI 4 and 5 were taken to indicate cancer and MRI 1,2 and 3 to indicate normal than if MRI 3 were to be included with 4 and 5 to indicate cancer. This is unsurprising because the use of the “3” category by a reader indicates that the reader is uncertain whether or not a cancer is present. It has previously been reported that in mammogram reporting 10-30% of breasts classified as “3” demonstrate a true cancer(21,22), and our study’s results fall within that range; of the 247 “3” classifications given by our readers, only 26 (11%) were cancers. Mammographic screening programmes recall “3” classifications for further imaging. This is necessary because mammographic techniques selectively pick up low-grade, biologically indolent cancers(23,24) so that choosing to ignore indeterminate abnormalities in mammographic screening is risky because small, high-grade, biologically aggressive cancers can have a subtle or indeterminate appearance on mammogram(25). In contrast, FAST MRI was originally designed to preferentially pick up the biologically aggressive cancers(11,26), and so choosing not to recall indeterminate findings from screening moderate risk women

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with FAST MRI might be less risky because aggressive cancers would be clearly seen as cancer. Whilst choosing to screen with FAST MRI rather than mammograms has the primary objective of reducing under-diagnosis, choosing not to recall indeterminate (“3”) FAST MRI findings might have the additional benefits of reducing both overdiagnosis and false positive recall rate(26). Reducing the number of screening assessments by reducing the number of women with normal breasts incorrectly recalled from screening would also reduce cost to the NHS.

Limitations of the study include that it uses an enriched dataset and not a real-life data series of screening cases, and therefore comparison of our results with those of screening studies is spurious. The creators of any enriched dataset determine its degree of difficulty, and therefore comparisons between readers of differently created datasets can be meaningless. As a consequence of the selection of cancers in our dataset being dependent on the indications for breast MRI at our institution, there were a very high proportion of lobular cancers included in our dataset ( $25/56 = 45\%$ ). This bias in our selection of cancer cases and our choice to limit the size of the included cancers increased the difficulty of the test we set our readers. In opposition to this effect, we chose not to include MRIs performed following a known cancer diagnosis that had originally been reported as MRI 1,2 or 3. This excluded cases that were occult on full protocol MRI, but since only 5 scans were excluded for this reason (Figure 1) the effect on reader results is not likely to be marked. In the UK both MRI and mammograms performed for breast screening are double-read, but in this study the dataset of FAST MRIs was single read, without access to previous examinations.

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Overall, we believe that the enriched data-set of FAST MRI images developed during this study is an effective and challenging test of performance at FAST MRI interpretation, and that the performance of readers when reading this dataset is likely to be an underestimate of their potential performance in screening practice, and may also be an underestimate of the difference between groups.

It may be considered a further limitation that the dataset of FAST MRI was acquired on a mixture of 1.5T and 3T scanners though this mixture of available equipment does reflect real life practice within NHSBSP, and a strength of this study is that both this mixture of scanners used and the mixture of multiprofessional readers that participated in the study represent the full range of scanners and of mammogram readers within NHSBSP at our centre.

The results of this study suggest that training mammogram readers to interpret FAST MRI may not take long, but allowance for longer interpretation times should be factored into workforce planning whilst they adapt to the new technology. Questions for future research include whether readers new to the technology can, with experience or additional training, speed up to the level achieved by expert MRI readers and how much additional experience or training is required to achieve adequate parity of performance.

## Conclusion

Overall, the results of this study, of a small sample of image readers, suggest that brief training of the whole NHSBSP image-reading workforce is likely to be sufficient to enable effective interpretation of FAST MRI in terms of accuracy and speed of interpretation.

Further studies, increasing the number of study participants (readers) and lengthening the training to a whole day of interactive teaching, are necessary to decide whether the difference between the groups can be further reduced and the overall accuracy and interpretation speed further improved prior to subsequent prospective studies of FAST MRI in a real-world screening setting.

A prospective study in real life screening practice is needed to determine whether choosing only to recall suspicious or malignant-appearing cases (MRI 4&5) on FAST MRI could be an effective strategy rather than the current standard of additionally recalling MRI 3 found on mammograms.

## Additional information (not included in word count)

### Consent for publication

Consent for publication of the MRI images included in this article has been obtained from the patients imaged.



### Availability of data and material

The datasets generated during the current study are not publicly available because the dataset has not yet been converted into an electronic form. The development of the dataset into an electronic form is the subject of a successful grant funding bid to NIHR. Once this has been achieved, and the dataset is in a readily shareable form, it will be available from the corresponding author on reasonable request.

### Conflict of interest

The authors declare no conflict of interest

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Figure and Table Legends

**Figure 1: Flow diagram to illustrate FAST MRI dataset**

**Figure 2: MRI classifications of each of the 250 breasts by the 8 image readers**

Figure 2a: 56 breasts with cancer

Figure 2b: 194 normal breasts

**Figure 3: Examples of FAST MRI images of breasts with cancer from the dataset**

Figure 3a: FAST MRI axial MIP image showing a Grade 3 invasive breast cancer (blue arrow) as an enhancing mass correctly classified as MRI 4 or 5 by 8/8 image readers.

The original clinical indication for breast MRI was “palpable cancer not visible (occult) on mammogram”

Figure 3b: FAST MRI axial MIP image showing High Grade ductal carcinoma in situ (DCIS) as asymmetric non-mass enhancement (blue arrows) correctly classified as MRI 4 or 5 by 7/8 image readers. This image also illustrates that the heart (paired arrows) and blood vessels exhibit enhancement on FAST MRI.

Figure 3c: FAST MRI axial slice from slice stack showing a lobular carcinoma (blue arrow) that showed only on this single slice from the slice stack and not on the MIP. This case was the only cancer from the dataset to be “missed” by 8/8 readers. This figure also demonstrates the appearance of movement artefact on subtracted images like FAST MRI. Movement artefact appears as adjacent black and white lines, together producing a “ghost-like” appearance (orange arrows). Movement artefact is likely to have contributed to the readers’ failure to perceive the lobular cancer.

**Table 1: Clinical indication for the MRI scans of the dataset**

**Table 2: Histology of cancers in dataset**

**Table 3: Comparison of readers' MRI classification against the true outcome**

**Table 4: Accuracy of the FAST MRI readers against the true outcome**

**Table 5: Individual Readers' Results when MRI classifications 4 and 5 are considered as cancers**